

FORM PTO-1449 U.S. Department of Commerce Patent and Trademark Office	Docket No. UCSD1140-1	Serial No.: 09/889,251
	Applicants: Robert K. Naviaux	
SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT	Filing Date: November 1, 2001	Group Art Unit: 1614 O P E S C L

**U.S. PATENT DOCUMENTS**

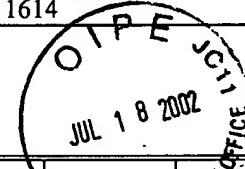
EXAM. INITIALS		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB- CLASS	FILING DATE
PS	AA	4,960,759	10/02/1990	De Luca et al.	514	50	
PS	AB	5,190,948	03/02/1993	Materazzi et al.	514	274	
PS	AC	5,470,838	11/28/1995	von Borstel and Bamat	514	50	
PS	AD	5,567,689	10/22/1996	Sommadossi and Kouni	514	50	
PS	AE	5,583,117	12/10/1996	von Borstel and Bamat	514	50	
PS	AF	5,691,320	11/25/1997	von Borstel et al.	514	50	
PS	AG	5,723,449	03/03/1998	Sommadossi and Kouni	514	50	
PS	AH	5,736,531	04/07/1998	von Borstel and Bamat	514	50	
PS	AI	5,852,000	12/22/1998	Ichihara and Yokoyama	514	45	
PS	AJ	5,962,459	10/05/1999	Piazza et al.	514	269	
PS	AK	6,258,795 B1	07/10/2001	von Borstel and Bamat	514	49	
PS	AL	2001/0016576 A1	08/23/2001	von Borstel, Reid W.	514	44	

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### FOREIGN PATENT DOCUMENTS



EXAM. INITIALS		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	PATENT & TRADEMARK OFFICE SUB-CLASS	TRANSLATION (YES/NO)
PS	AM	WO 00/11952	03/09/2000	PCT			
PS	AN	WO 00/50043	08/31/2000	PCT			

### OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages)

PS	AO ✓	Ashour, O.M. et al., "5-(m-Benzylxybenzyl) Barbituric Acid Acyclonucleoside, A Uridine Phosphorylase Inhibitor, and 2', 3', 5'-tri-O-Acetyluridine, A Prodrug of Uridine, As Modulators of Plasma Uridine Concentration. Implications for Chemotherapy." <i>Biochem Pharmacol.</i> , Vol. 51, No. 12, June 1996, pgs. 1601-1611, (Abstract).
PS	AP ✓ 6	Bjornberg, O. et al., "The Activity of Escherichia Coli Dihydroorotate Dehydrogenase Is Dependent On a Conserved Loop Identified By Sequence Homology, Mutagenesis, and Limited Proteolysis," <i>Biochemistry</i> , Vol. 38, No. 10, March 9, 1999, (Abstract) pgs. 2899-2908.
	AQ	Brinkman, K. et al., "Adverse Effects of Reverse Transcriptase Inhibitors: Mitochondrial Toxicity As Common Pathway," <i>AIDS</i> , Vol. 12, No. 14, October 1, 1998, (Abstract) pgs. 1735-1744.
PS	AR ✓	Bruneau, J.M. et al., "Purification of Human Dihydro-Orotate Dehydrogenase and Its Inhibition by a A77 1726, the Active Metabolite of Leflunomide," <i>Biochem. J.</i> , Vol. 336, Part 2, December 1, 1998, (Abstract) pgs. 299-303.
PS	AS ✓	Chariot, P. et al., "Zidovudine-Induced Mitochondrial Disorder with Massive Liver Steatosis, Myopathy, Lactic Acidosis, and Mitochondrial DNA Depletion," <i>J. Hepatol.</i> , Vol. 30, No. 1, January 1999, (Abstract) pgs. 156-160.
PS	AT ✓	Cheong H.I. et al., "Hereditary Glomerulopathy Associated With A Mitochondrial tRNA (Leu) Gene Mutation," <i>Pediatr. Nephrol.</i> , Vol. 13, No. 6, August 1999, (Abstract) pgs. 477-480.

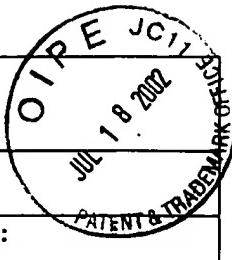
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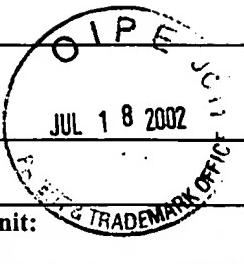
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<i>RS</i>	AU	Connolly, Gerald P., "Abnormal Pyrimidine Metabolism Is the Basis of Some Neurological Diseases," <i>Trends Pharmacol. Sci.</i> , Vol. 19, No. 7, July 1998, pg. 252.
<i>RS</i>	AV	Connolly, Gerald P. et al., "Pyrimidines and CNS Regulation," and "McLeod et al. Reply". <i>TIPS</i> , Vol. 17, No. 1, March 1996, pgs. 106-107.
<i>RS</i>	AW	Connolly and Duley, "Uridine and Its Nucleotides: Biological Actions, Therapeutic potentials," <i>TIPS</i> , Vol. 20, May 1999, pgs. 218-225.
<i>RS</i>	AX	Costanzi-Strauss, E. et al., "Restoration of Growth Arrest By a p16INK4, p21WAF1, pRB, and p53 is Dependent on the Integrity of the Endogenous Cell-Cycle Control Pathways In Human Glioblastoma Cell Lines," <i>Exp. Cell Res.</i> , Vol. 238, No. 1, January 10, 1998, (Abstract) pgs. 51-62.
<i>RS</i>	AY	Damore, M.E. et al., "Early Onset of Diabetes Mellitus Associated With the Mitochondrial DNA T14709C Point Mutation: Patient Report and Literature Review," <i>J. Pediatr. Endocrinol. Metab.</i> , Vol. 12, No. 2, March-April 1999, (Abstract) pgs. 207-213.
	AZ	De la Asuncion, J.G. et al., "Zidovudine (AZT) Causes an Oxidation of Mitochondrial DNA In Mouse Liver," <i>Hepatology</i> , Vol. 29, No. 3, March 1999, (Abstract) pgs. 985-987.
<i>RS</i>	BA	De la Asuncion, J.G. et al., "AZT Treatment Induces Molecular and Ultrastructural Oxidative Damage to Muscle Mitochondria. Prevention By Antioxidant Vitamins," <i>J. Clin. Invest.</i> , Vol. 102, No. 1, July 1998, (Abstract) pgs. 4-9.
<i>RS</i>	BB	De Muys, J.M. et al., "Anti-Human Immunodeficiency Virus Type 1 Activity, Intracellular Metabolism, and Pharmacokinetic Evaluation of 2'-deoxy-3'-oxa-4'-thiocytidine," <i>Antimicrob. Agents Chemother.</i> , Vol. 43, No. 8, August 1999, (Abstract) pgs. 1835-1844.
<i>RS</i>	BC	Fox, R.I., "Mechanism of Action of Leflunomide In Rheumatoid Arthritis," <i>J. Rheumatol. Suppl.</i> , Vol. 53, July 1998, (Abstract) pgs. 20-26.
<i>RS</i>	BD	Graff, C. et al., "Mitochondrial Medicine—Recent Advances," <i>J. Intern. Med.</i> , Vol. 246, No. 1, July 1999, (Abstract) pgs. 11-23.
<i>RS</i>	BE	Gregoire, Michel et al., "On Auxotrophy for Pyrimidines of Respiration-Deficient Chick Embryo Cells," <i>Euro. J. Biochem.</i> , Vol. 142, 1984, pgs. 49-55.

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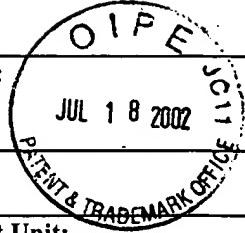


AS	BF	Janssen, G.M. et al., "The Diabetes-Associated 3243 Mutation In the Mitochondrial tRNA (Leu(UUR)) Gene Causes Severe Mitochondrial Dysfunction Without A Strong Decrease In Protein Synthesis Rate," <i>J. Biol. Chem.</i> , Vol. 274, No. 42, October 15, 1999, (Abstract) pgs. 29744-29748.
PS	BG	Jockel, J. et al., "Structural and Functional Comparison of Agents Interfering with Dihydroorotate, Succinate and NADH Oxidation of Rat Liver Mitochondria," <i>Biochem. Pharmacol.</i> , Vol. 56, No. 8, October 15, 1998, (Abstract) pgs. 1053-1060.
PS	BH	Kelsen, David P. et al., "Phase I Trial of PN401, an Oral Prodrug of Uridine, to Prevent Toxicity From Fluorouracil in Patients with Advanced Cancer," <i>Journal of Clinical Oncology</i> , Vol. 15, No. 4, April 1997, pgs. 1511-1517.
PS	BI	Knecht and Loffler, "Species-Related Inhibition of Human and Rat Dihydroorotate Dehydrogenase By Immunosuppressive Isoxazol and Chinchoninic Acid Derivative," <i>Biochem. Pharmacol.</i> , "Vol. 56, No. 9, November 1998, (Abstract) pgs. 1259-1264.
PS	BJ	Kraft, J. et al., "Biological Effects of the Dihydroorotate Dehydrogenase Inhibitor Polyporic Acid, A Toxic Constituent of the Mushroom Hapalopilus Rutilans, In Rats and Humans," <i>Arch. Toxicol.</i> , Vol. 72, No. 11, November 1998, (Abstract) pgs. 711-721.
PS	BK	Lehto, M. et al., "High Frequency of Mutations In MODY and Mitochondrial Genes In Scandinavian Patients With Familial Early-Onset Diabetes," <i>Diabetologia</i> , Vol. 42, No. 9, September 1999, (Abstract) pgs. 1131-1137.
PS	BL	Loffler, M. et al., "Dihydroorotate-Ubiquinone Oxidoreductase Links Mitochondria In the Biosynthesis of Pyrimidine Nucleotides," <i>Mol. Cell Biochem.</i> , Vol. 174., 1997, pgs. 125-129.
PS	BM	Masanés, F. et al. "Clinical, Histological and Molecular Reversibility of Zidovudine Myopathy," <i>J. Neurol. Sci.</i> , Vol. 159, No. 2, August 14, 1998, (Abstract) pgs. 226-228.
PS	BN	Masini, A. et al., "Zidovudine-Induced Experimental Myopathy: Dual Mechanism of Mitochondrial Damage," <i>J. Neurol. Sci.</i> , Vol. 166, No. 2, July 1, 1999, (Abstract) pgs. 131-140.
PS	BO	Matsuura, N. et al., "The prevalence of Mitochondrial Gene Mutations In Childhood Diabetes In Japan," <i>J. Pediatr. Endocrinol. Metab.</i> , Vol. 12, No. 1, January-February 1999, (Abstract) pgs 27-30.

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PS	BP 6	Morris, A.A., "Mitochondrial Respiratory Chain Disorders and the Liver," <i>Liver</i> , Vol. 19, No. 5, October 1999, (Abstract) pgs. 357-368.
PS	BQ 4	Nakamura S. et al., "Renal Complications In Patients With Diabetes Mellitus Associated With an A to G Mutation of Mitochondrial DNA at the 3243 Position of Leucine tRNA," <i>Diabetes Res. Clin. Pract.</i> , Vol. 44, No. 3, June 1999, (Abstract) pgs. 183-189.
PS	BR 6	Naviaux, R. K. et al., "Clinical Experience with Uridine and Triacetyluridine (PN401) Therapy of Mitochondrial Disease," <i>Presented at the "Mitochondrial Dysfunction in Human Pathology" meeting Melbourne, Australia</i> , September 7, 1998.
PS	BS 6	Naviaux, R.K. et al., "Sensitive Assay for Mitochondrial DNA Polymerase Gamma," <i>Clin. Chem.</i> , Vol. 45, No. 10, October 1999, (Abstract) pgs. 1725-1733.
	BT	Naviaux, R.K. et al., "Mitochondrial DNA Polymerase Gamma Deficiency and mtDNA Depletion In a Child with Alpers' Syndrome," <i>Ann. Neurol.</i> , Vol. 45, No. 1, January 1999, (Abstract) pgs. 54-58.
PS	BU 8	Naviaux, R.K. et al., "Correction of Renal Tubular Acidosis (RTA) in Mitochondrial Disease Patients Treated with Triacetyluridine (PN401)," <i>Abstract Submitted for Presentation, Society for Inherited Metabolic Disorders Annual Meeting</i> , March 12-15, 1999.
PS	BV 6	Otabe, S. et al., "Molecular and Historical Evaluation of Pancreata From Patients with a Mitochondrial Gene Mutation Associated with Impaired Insulin Secretion," <i>Biochem. Biophys. Res. Commun.</i> , Vol. 259, No. 1, May 1999, (Abstract) pgs. 149-156.
PS	BW 6	Page, Theodore et al., "Developmental Disorder Associated With Increased Cellular Nucleotidase Activity," <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 94, October 1997, pgs. 11601-11606.
PS	BX 6	Pizzorno, G. et al., "Phase I Clinical and Pharmacological Studies of Benzylacyclouridine, A Uridine Phosphorylase Inhibitor," <i>Clin. Cancer Res.</i> , Vol. 4, No. 5, May 1998, (Abstract) pgs. 1165-1175.
PS	BY 6	Ruckemann, K. et al., "Leflunomide Inhibits Pyrimidine de Novo Synthesis In Mitogen-Simulated T-Lymphocytes from Healthy Humans," <i>J. Biol. Chem.</i> , Vol. 273, No. 34, August 21, 1998, (Abstract) pgs. 21682-21691.

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PS	BZ	Schwartz et al., "Oral Triacetyluridine (TAU) as A Rescue Agent for 5-Fluotouracil (5FU): Phase I and Pharmacological Study," <i>Proc. Am. Soc. Clin. Oncol.</i> , (13, 30 Meet., 134, 1994), Abstract.
PS	CA	Smith P.R. et al., "Pigmentary Retinal Dystrophy and the Syndrome of Maternally Inherited Diabetes and deafness Caused By the Mitochondrial DNA 3243 tRNA (Leu) A to G Mutation," <i>Ophthalmology</i> , Vol. 106, No. 6, June 1999, (Abstract) pgs. 1101-1108.
PS	CB	Szabados, E. et al., "Role of Reactive Oxygen Species and Poly-ADP-Ribose Polymerase In the Development of AZT-Induced Cardiomyopathy In Rat," <i>Free Radic. Biol. Med.</i> , Vol. 26, No. 3-4, February 1999, (Abstract) pgs. 309-317.
PS	CC	van Groeningen, C.J. et al., "Clinical and Pharmacologic Study of Orally Administered Uridine," <i>Journal of the National Cancer Institute</i> , Vol. 83, No. 6, March 20, 1991, pgs.437-441.
PS	CD	van Groeningen, C.J. et al., "Modulation of Fluorouracil Toxicity with Uridine," <i>Semin. Oncol.</i> , Vol. 19, 2 Supp. 3, 1992, (Abstract) pgs. 148-154.
PS	CE	Yu, Alice L. et al., "Pyrimidine Responsive Syndrome of Neurologic Dysfunction and Susceptibility to Infection," <i>Ped Res</i> , Vol. 41, 1997, Abstract, pg. 639.

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